UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	0327-0759-0
First Inventor or Application Identifier	Naoko TSUJI, et al.
Title	METHOD OF INHIBITING HAIR GROWTH

JC541 U.S. PTO 09/222691 12/28/98

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APPLICATION ELEMENTS
See MPEP chapter 600 concerning utility patent application contents

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Fee Transmittal Form (e.g. PTO/SB/17)
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■ Specification — Total Pages: 23

3. ■ Drawing(s) *(35 U.S.C. 113)* — Total Sheets: 1

4. ■ Oath or Declaration — Total Pages: 4
   a. ■ Newly executed (original)
   b. □ Copy from a prior application *(37 C.F.R. §1.63(d))*
   (for continuation/divisional with box 15 completed)
      i. □ DELETION OF INVENTOR(S)
      Signed statement attached deleting inventor(s) named in the prior application, see *37 C.F.R. §1.63(d)(2) and 1.33(b).*

5. □ Incorporation By Reference *(usable if box 4B is checked)*
The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4B, is considered to be part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

ACCOMPANYING APPLICATION PARTS

6. □ Assignment Papers (cover sheet & document(s))
7. □ 37 C.F.R. §3.73(b) Statement *(when there is an assignee)* □ Power of Attorney
8. □ English Translation Document *(if applicable)*
9. □ Information Disclosure Statement (IDS)/PTO-1449 □ Copies of IDS Citations
10. □ Preliminary Amendment
11. ■ White Advance Serial No. Postcard
12. □ Small Entity Statement(s) □ Statement filed in prior application, Status still proper and desired.
13. ■ Certified Copy of Priority Document(s) (1)
(if foreign priority is claimed)
14. ■ Other: Notice of Priority

15. If a CONTINUING APPLICATION, *check appropriate box, and supply the requisite information below:*
□ Continuation □ Divisional □ Continuation-in-part (CIP) of prior application no.:
Prior application information: Examiner: Group Art Unit:

16. Amend the specification by inserting before the first line the sentence:
□ This application is a □ Continuation □ Division □ Continuation-in-part (CIP)
of application Serial No. Filed on

□ This application claims priority of provisional application Serial No. Filed

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Docket No. 0327-0759-0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTOR(S) Naoko TSUJI, et al.

SERIAL NO: New Application

FILING DATE: Herewith

FOR: METHOD OF INHIBITING HAIR GROWTH

FEE TRANSMITTAL

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Respectfully Submitted,

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TITLE OF THE INVENTION:

METHOD OF INHIBITING HAIR GROWTH

BACKGROUND OF THE INVENTION

Field of the Invention:

The present invention relates to a method of inhibiting hair growth, and more particularly to a method of inhibiting hair growth, by which hair growth on the legs and arms, and the like can be effectively inhibited, and use of a specific enzyme inhibitor for the preparation of a hair-growth inhibitor.

Description of the Background Art:

A biological function of the scalp hair and body hair is to protect important organs of the head, chest, limbs and the like. With the development of clothes and protecting means, however, the organ-protecting function carried by the body hair has come to be unimportant.

The scalp hair is generally desired to be thick. In recent years, however, the tendency to prefer having no hair on, particularly, limbs and the like has been strengthened from the viewpoint of an aesthetic appearance. Therefore, various methods for removing the body hair have been developed and used. Specific examples thereof include mechanical removing methods making use of a shaver, hair plucker or the like, methods of using a depilatory to depilate body hair out of its root, methods of using a hair remover to remove body hair

by its chemical reaction, etc.

However, these methods for removing the body hair are accompanied by the physical or chemical irritation of the skin, and the lastingness of their removing effects on the body hair is limited even though there is some difference between the methods. Therefore, such a treatment for removing the body hair must be conducted again after a certain period of time. It is thus desired to lighten the removal treatment of the body hair.

International Application WO98/25580 published June 18, 1998 discloses a method for reducing hair growth by inhibiting the activity of a matrix metalloproteinase in the skin. The present invention intends the same purpose, i.e., providing a method of inhibiting hair growth. However, the researchers of the present invention found that hair growth is deeply influenced by the activity of elastase-like enzymes. Thus, there is fundamental difference in the present invention from the prior art, which provides a novel method characterized by inhibition of the activity of elastase-like enzymes.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a method of inhibiting hair growth, by which the growth of body hair can be effectively inhibited to reduce the number of removal treatments of the body hair.

In view of the foregoing circumstances, the present inventors have carried out an extensive investigation. As a result, it has been quite surprisingly found that inhibitors of elastase-like enzymes which digest elastin known as a structural protein in the artery, tendon, skin or the like, and inhibitors of neutral endopeptidases that are enzymes which digest opioid peptides such as enkephalin, and neuropeptides such as substance P and bradykinin have an excellent inhibitory effect on hair growth, thus leading to completion of the present invention.

According to the present invention, there is thus provided a method of inhibiting hair growth, which comprises administering an inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor.

According to the present invention, there is also provided use of an inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor for the preparation of a hair-growth inhibitor.

According to the present invention, an excellent inhibitory effect on hair growth can be achieved, and hair-growth inhibitors high in safety for the human body can also be provided.

BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 diagrammatically illustrates the relationship between a hair cycle and the activity of an

elastase in cutaneous tissue.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

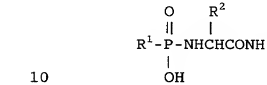
As the inhibitor of elastase-like enzymes useful in the practice of the present invention, is preferred an elastase inhibitor, particularly, an inhibitor of elastase-like enzymes derived from a dermoepidermal fibroblast. Such inhibitors include substances which exhibit an inhibitory activity of at least 50% at 1 mM in an enzyme activity-measuring system making use of an enzyme solution extracted from, for example, cultured human fibroblasts with a 0.1% Triton X-100/0.2 M Tris-hydrochloric acid buffer solution (pH: 8.0) and containing N-succinyl-Ala-Ala-Ala-p-nitroanilide as a substrate.

As the neutral endopeptidase inhibitor useful in the practice of the present invention, is preferred an inhibitor of a neutral endopeptidase derived from a dermoepidermal fibroblast. Such inhibitors include substances which exhibit an inhibitory activity of at least 50% at 1 mM in an enzyme activity-measuring system making use of an enzyme solution extracted from, for example, cultured human fibroblasts with a 0.1% Triton X-100/0.2 M Tris-hydrochloric acid buffer solution (pH: 8.0) and containing glutaryl-Ala-Ala-Phe-4-methoxy-2-naphthylamine as a substrate in an MES (2-morpholino-ethane sulfonic acid) buffer solution (100 mM, pH: 6.5)

to which sodium chloride (300 mM) has been added.

Examples of such elastase-like enzyme inhibitors or neutral endopeptidase inhibitors include phosphonic acid derivatives, mercaptopropionamide derivatives and salts thereof.

The phosphonic acid derivatives include compounds represented by the following general formula (1):



(1)

wherein R^1 is a hydrogen atom, a hydroxyl group, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted, R^2 is a hydrogen atom, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted, and R^3 is a hydrogen atom or a $-CH(R^4)COOH$ (in which R^4 is a hydrogen atom or a hydrocarbon group which may be substituted), and salts thereof.

In the formula (1), the hydrocarbon groups which are represented by R^1, R^2 and R^4 and may be substituted may be either saturated hydrocarbon groups or unsaturated hydrocarbon groups, and examples thereof include alkyl, alkenyl, alkynyl, cyclic alkyl, cyclic alkenyl, aromatic hydrocarbon and aralkyl groups. These hydrocarbon groups preferably have 1 to 24 carbon atoms, particularly 1 to 18 carbon atoms.

Of the hydrocarbon groups represented by R^1, R^2 and

R^4, the alkyl, cyclic alkyl, aromatic hydrocarbon and aralkyl groups are preferred. The alkyl groups are preferably linear or branched alkyl groups having 1 to 12 carbon atoms, with n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl and isoamyl groups being more preferred. The cyclic alkyl groups are preferably 5- to 7-membered alicyclic alkyl groups, with cyclopentyl and cyclohexyl group being more preferred. The aromatic hydrocarbon groups are preferably aromatic hydrocarbon groups having 6 to 14 carbon atoms, such as phenyl and naphthyl groups. The aralkyl groups are preferably alkyl groups having 1 to 5 carbon atoms, which have been substituted by an aromatic hydrocarbon group having 6 to 12 carbon atoms, and examples thereof include 2-phenylethyl (= phenethyl), 2-(1-naphthyl)ethyl and 2-(2-naphthyl)ethyl groups.

Examples of atoms or groups which may be substituted on the hydrocarbon groups represented by R^1, R^2 and R^4 include halogen atoms, a hydroxyl group, alkoxyl groups, acyl groups, an amino group which may be protected, and heterocyclic groups. The halogen atoms include chlorine, bromine and iodine atoms. The alkoxyl groups are preferably alkoxyl groups having 1 to 12 carbon atoms, and examples thereof include methoxy, ethoxy and isopropoxy groups. The acyl groups are preferably alkanoyl groups having 1 to 12 carbon atoms, and examples thereof include acetyl, propionyl and butyryl groups. Examples of the amino group which may be

protected include amino, C_{1-8}-acylamino and C_{1-6}-alkylamino di-(C_{1-6}-alkyl)amino groups. The heterocyclic groups are preferably 5- to 14-membered monocyclic or fused ring groups having, as heteroatom(s), 1 to 3 nitrogen, oxygen and/or sulfur atoms, and examples thereof include pyridyl, pyridazinyl, furyl, thienyl, indolyl, thiazolyl, imidazolyl, benzofuryl and benzothienyl groups.

The sugar residues include monosaccharide residues and oligosaccharide residues. Examples of groups which may be substituted on these sugar residues include alkyl, acyl and aralkyl groups. Examples of the alkyl, acyl and aralkyl groups include the same C_{1-12} alkyl, C_{1-6} acyl and C_{6-12}-aryl-C_{1-6}-alkyl groups as mentioned above.

These phosphonic acid derivatives can be prepared in accordance with, for example, the process described in Japanese Patent Application Laid-Open No. 105698/1993.

The mercaptopropionamide derivatives include, for examples, compounds represented by the following general formula (2):

$$R^5\text{-}SCH_2\underset{\displaystyle R^6}{\underset{|}{C}}HCONH(CH_2)_n\text{-}R^7 \qquad (2)$$

wherein R^5 is a hydrogen atom or an acyl group, R^6 is a hydrogen atom or a hydrocarbon group which may be substituted, R^7 is a hydrogen atom, a carboxyl group, an alkoxycarbonyl group, a hydrocarbon group which may be substituted, a heterocyclic group which may be substituted, or an acyl group, and n is a number of 1 to

20.

In the formula (2), the acyl groups represented by R^5 and R^7 include alkanoyl groups and arylcarbonyl groups. The alkanoyl groups are preferably alkanoyl groups having 1 to 12 carbon atoms, and examples thereof include acetyl, propionyl and butyryl groups. The arylcarbonyl groups are preferably having 7 to 15 carbon atoms, and examples thereof include benzoyl, substituted benzoyl, naphthylcarbonyl and substituted naphthylcarbonyl groups. Examples of groups or atoms substituted on the benzoyl and naphthylcarbonyl groups include C_{1-6} alkyl groups, C_{1-6} alkoxyl groups, halogen atoms, an amino group, a hydroxyl group and C_{1-6} alkanoyloxy groups. n is preferably 1 to 6, more preferably 1 or 2.

The hydrocarbon groups which are represented by R^6 and R^7 and may be substituted include the same groups as those mentioned above as to R^1, R^2 and R^4.

The heterocyclic group represented by R^7 is preferably a 5- to 14-membered monocyclic or fused ring group having, as heteroatom(s), 1 to 3 nitrogen, oxygen and/or sulfur atoms, and examples thereof include pyridyl, pyridazinyl, furyl, thienyl, indolyl, thiazolyl, imidazolyl, benzofuryl, benzothienyl, pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl groups. Examples of atoms or groups which may be substituted on the heterocyclic group include halogen atoms, a hydroxyl group, alkoxyl groups, acyl groups and an amino group

which may be protected. Specific examples of these substituents include the same substituents as the substituents of the hydrocarbon groups mentioned above as to R^1, R^2 and R^4.

The alkoxycarbonyl group represented by R^7 includes alkoxycarbonyl groups the alkoxy moiety of which has 1 to 12 carbon atoms, and specific examples thereof include methoxycarbonyl, ethoxycarbonyl, isopropoxycarbonyl and butoxycarbonyl groups.

These mercaptopropionamide derivatives can be prepared in accordance with, for example, the process described in Japanese Patent Application Laid-Open No. 24354/1982. Incidentally, these mercaptopropionamide derivatives are known to have an inhibitory effect on mammalian collagenases, but not known at all to have an inhibitory effect on elastase-like enzymes.

The phosphonic acid derivatives and mercapto-propionamide derivatives may be used in the form of pharmaceutically acceptable salts or hydrates. Examples of the salts include alkali metal salts, alkaline earth metal salts, organic amine salts and amino acid salts. Examples of the alkali metal salts include the sodium salt and potassium salt. The examples of the alkaline earth metal salts include the calcium salt and magnesium salt. Examples of the organic amine salts include the ammonium salts, methylamine salt, triethylamine salt and pyridinium salt. Examples of the amino acid salts

include the arginine salt, lysine salt and histidine salt. The alkali metal salts and amino acid salts are more preferred. As sites at which a salt is formed, may be mentioned the moieties of the phosphonic acid residue and carboxyl group in the phosphonic acid derivatives and the moieties of the thiol group and carboxyl group in the mercaptopropionamide derivatives. In the case where a salt is formed, the salt may be formed at both or one of these residues.

No particular limitation is imposed on the hair-growth inhibitor useful in the practice of the present invention. However, it is preferably used in the form of an external skin-care composition, particularly, a cosmetic composition related to hair removal, depilation or shaving. Specific examples of such a cosmetic composition include hair removers in the form of paste, cream or aerosol, depilatories in the form of wax, gel or sheet, after-treatment compositions used for a treatment after hair removal or depilation, such as lotion and cream, antiperspirant and deodorant cosmetics such as deodorant lotion, deodorant powder, deodorant spray and deodorant stick, treatment compositions before shaving, such as pre-shave lotion, shaving compositions such as shaving cream, and treatment compositions after shaving, such as after-shave lotion.

It is preferred that the amount of the active ingredient incorporated into the hair-growth inhibitor

according to the present invention be generally 0.0001 to 10 % by weight, particularly, 0.001 to 3 % by weight based on the total weight of the inhibitor from the viewpoints of the inhibitory effect on hair growth, profitability, etc.

In the hair-growth inhibitor according to the present invention, various optional ingredients commonly used for cosmetics, quasi-drugs and drugs may be suitably incorporated as needed so far as no detrimental influence is thereby imposed on the effects of the present invention. Examples of such optional ingredients include purified water, ethanol, oily substances, moisturizers, thickeners, preservatives, emulsifiers, medicinally-effective agents, powders, ultraviolet absorbents, pigments, perfume bases and emulsion stabilizers.

Example 1:

[Hair cycle and elastase activity]

After a fascia was removed from the shaved back skin of each of SD rats (male) aged 5 weeks to 13 weeks that were in various hair-growing stages, cutaneous tissue specimens 4 mm in diameter were prepared. A phosphate buffer solution (PBS) was then put in a peripheral part of a Petri dish for organ culture (Falcon 3037) for the purpose of keeping humidity constant, and the cutaneous tissue specimens (6 tissue specimens/dish) were arranged on a triangular grid placed on an inner dish with the epidermis upside. A liquid medium

(Dulbecco's Modified Eagle Medium (DMEM), 0.7 ml) was added into the inner dish to conduct culture at 31°C for 24 hours in a gas phase of 60% O_2 and 5% CO_2. The thus-obtained culture supernatant was used for the measurement of elastase activity.

The measurement of elastase activity was conducted in accordance with the method by Bieth et al. [Biochem. Biophys. Res. Commun., 53, 383-390 (1973)]. More specifically, a 20 mM solution of N-succinyl-$(Ala)_3$-p-nitroanilide was used as a substrate and added in a proportion of 5 µl per 95 µl of the culture supernatant. A reaction was conducted at 37°C for 4 hours, and an absorbance at 410 nm was measured, thereby determining the amount of nitroaniline formed by the reaction with the enzyme. With respect to the enzyme activity, the activity that 1 nmol per hour of nitroaniline is formed was regarded as 1 unit.

As apparent from the result shown in Fig. 1, the rise and fall of the activity of an elastase in the cutaneous tissue released in the culture supernatant very much corresponded to the hair cycle thereof. More specifically, a high value was exhibited in a hair follicle-forming phase (growth phase), and a fall in activity value was recognized in a transient phase or resting phase. This result suggests that a rise in the activity of the elastase in the cutaneous tissue is indispensable to hair follicle formation and its growth.

Test Example 1: Elastase activity-inhibiting test in cultured human fibroblast

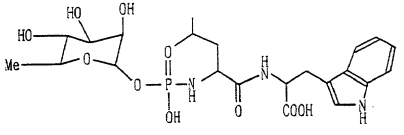
Normal human fibroblasts commercially available from Dainippon Pharmaceutical Co., Ltd. were subcultured in a DMEM containing a 10% fetal bovine serum and used in this test. The cells separated from a Petri dish with a rubber policeman were suspended in physiological saline, collected by means of a low-speed centrifugal separator and washed 3 times with physiological saline. The thus-treated cells were suspended in a 0.1% Triton X-100/0.2 M Tris-HCl buffer (pH: 8.0) and ultrasonically disrupted to use as an enzyme solution.

125 mM N-Succinyl-$(Ala)_3$-p-nitroanilide was used as a substrate for the measurement of enzyme activity, and each subject (1 μl; its concentration is shown in Table 1) was added to the enzyme solution (100 μl) to conduct a reaction at 37°C for 1 hour. The reaction was stopped by adding acetic acid (5 μl). The amount of nitroaniline formed was determined by measuring an absorbance at 405 nm by means of a spectrophotometer. Percent inhibition of elastase activity by the subject is shown in Table 1.

Table 1

Subject	Concentration	Percent inhibition of elastase activity (%)
Compound 1	0.1 mM	85.6
Compound 2	0.1 mM	82.1
Compound 3	0.1 mM	90.2
Compound 4	1 mM	68.4
Compound 5	0.1 mM	90.1
Compound 6	0.1 mM	88.7
Compound 7	0.1 mM	85.4
Compound 8	0.1 mM	89.6

Compound 1:



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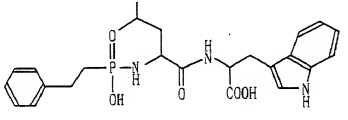

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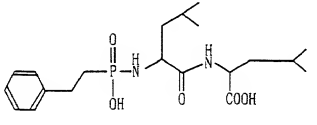

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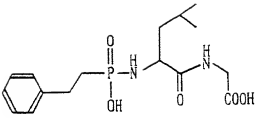

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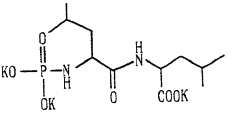

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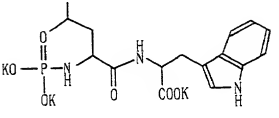
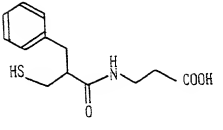
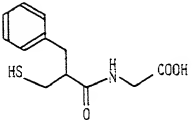


Compound 7:



Compound 8:



Test Example 2: Neutral endopeptidase activity-inhibiting test in cultured human fibroblast

Normal human fibroblasts commercially available from Dainippon Pharmaceutical Co., Ltd. were subcultured in a DMEM containing a 10% fetal bovine serum and used in this test. The cells separated from a Petri dish with a

rubber policeman were suspended in phosphate- buffered physiological saline, collected by means of a low-speed centrifugal separator and washed 3 times with phosphate-buffered physiological saline. The thus- treated cells were suspended in a 0.1% Triton X-100/0.2 M Tris-HCl buffer (pH: 8.0) and ultrasonically disrupted to use as an enzyme solution.

The enzyme solution (2 μl), a solution (1 μl) of each subject compound and 20 mM glutaryl-Ala-Ala-Phe-4-methoxy-2-naphthylamine as a substrate for the measurement of enzyme activity were added to 100 μl of an MES buffer solution (100 mM, pH: 6.5), to which sodium chloride (300 mM) had been added, to conduct a reaction at 37°C for 1 hour. The reaction was stopped by adding phosphoramidone so as to give a final concentration of 0.4 μM. Aminopeptidase M was added to the reaction mixture so as to give a final concentration of 20 mU, thereby conducting a reaction at 37°C for 15 minutes. The amount of 4-methoxy-2-naphthylamine formed was determined by measuring a fluorescence intensity at an excitation wavelength of 340 nm and a fluorescence wavelength of 425 nm by means of a fluorescence spectrophotometer, thereby finding percent inhibition of neutral endopeptidase activity by the subject compound. The percent inhibition of neutral endopeptidase activity by the subject is shown in Table 2.

Table 2

Subject	Concentration	Percent inhibition of neutral endopeptidase activity (%)
Compound 1	10 μM	99.0
Compound 2	10 μM	98.8
Compound 7	10 μM	97.1
Compound 8	10 μM	96.3

Test Example 3: Test of inhibiting regeneration of mouse back hair

Back hair of a group of 5 C3H mice aged 6 weeks was shaved over 2 x 4 cm^2 by means of an electric hair clipper and an electric shaver so as not to damage their skins. Each subject was applied to the shaved sites twice a day in an amount of 100 μl/time over 4 weeks. The subject was dissolved in a solvent (80% ethanol) to prepare a solution of a concentration shown in the following Table 3. Only the solvent was applied to a control group. After 3 weeks, a photograph of each shaved site was taken at a fixed magnification for observing the state of regenerated hair to compare a regenerated hair area ratio (regenerated hair area/shaved area) of the test group with that of the control group. The results are shown in Table 3.

Table 3

Subject	Concentration	Percent inhibition of hair growth after 3 weeks from shaving (%)
Compound 1	1 mM	58.7
Compound 2	1 mM	59.1
Compound 3	1 mM	64.8
Compound 4	10 mM	60.5
Compound 5	1 mM	74.2
Compound 6	1 mM	62.1
Compound 7	1 mM	59.7
Compound 8	1 mM	71.6

As apparent from Tables 1 to 3, the subjects, which are elastase inhibitors or neutral endopeptidase inhibitors, had an excellent inhibitory effect on hair growth.

Example 2: Hair growth inhibiting lotion

		(wt.%)
A	Polyoxyethylene hardened castor oil	0.8
	Ethanol	30.0
B	Compound 2	1.0
	Sodium dodecylsulfate	0.12
	Dodecylmethylamine oxide	0.18
	Isopropyl alcohol	15.0
	Benzyl alcohol	15.0
	Glycerol	2.0

	Purified water	Balance

The components belonging to A were dissolved, and the components belonging to B were separately dissolved. The solution of B was added to the solution of A to uniformly stir and mix both solutions, thereby obtaining a hair growth inhibiting lotion.

Example 3: Hair growth inhibiting cream

		(wt.%)
A	Liquid paraffin	10.0
	Squalane	7.0
	Jojoba oil	3.0
	Solid paraffin	3.0
	Polyoxyethylene cetyl ether	2.0
	Sorbitan sesquioleate	1.0
	Potassium hydroxide	0.1
B	Compound 7	1.0
	Glycerol	3.0
	Ethylparaben	0.1
	Purified water	Balance

The components belonging to A were heated to melt them, and the components belonging to B were separately heated to melt them. The melt of B was added to the melt of A to uniformly stir and mix both melts, thereby emulsifying them. The resultant emulsion was then cooled to obtain a hair growth inhibiting cream.

Example 4: Hair growth inhibiting foam

		(wt.%)
A	Compound 8	1.0
	Cetanol	0.1
	Propylene glycol	2.0
	Dimethyl silicone oil	2.0
	Polyoxyethylene hardened castor oil	2.5
	Liquid paraffin	1.0
	Polyvinyl pyrrolidone	0.5
	Methylparaben	0.2
	Ethanol	10.0
	Purified water	Balance
B	Liquefied petroleum gas (propellant)	4.0

The components belonging to A were uniformly mixed and placed in a container. The component of B was charged into the container in accordance with a method known *per se* in the art to obtain a hair growth inhibiting foam.

Example 5: Aerosol

		(wt.%)
A	Compound 1	1.0
	Cetanol	1.2
	Propylene glycol	4.0
	Ethanol	8.0
	Purified water	Balance
B	Liquefied petroleum gas (propellant)	4.0

The components belonging to A were uniformly mixed and placed in a container. The component of B was

charged into the container in accordance with a method known *per se* in the art to obtain an aerosol.

Japanese Patent Application No. 10-005959, filed on January 14, 1998, is incorporated herein by reference in its entirety.

WHAT IS CLAIMED IS:

1. A method of inhibiting hair growth, which comprises administering an inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor.

2. The method according to Claim 1, wherein the inhibitor of elastase-like enzymes is another inhibitor of elastase-like enzymes than a matrix metalloproteinase inhibitor.

3. The method according to Claim 1, wherein the inhibitor of elastase-like enzymes is an inhibitor of an elastase-like enzyme derived from a dermoepidermal fibroblast.

4. The method according to Claim 1, wherein the neutral endopeptidase inhibitor is an inhibitor of a neutral endopeptidase derived from a dermoepidermal fibroblast.

5. The method according to Claim 1, wherein the enzyme inhibitor is topically administered to an area desired to inhibit hair growth.

ABSTRACT OF THE DISCLOSURE

Disclosed herein are a method of inhibiting hair growth, which comprises administering an inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor, and use of an inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor for the preparation of a hair-growth inhibitor.

Fig. 1

n=3
Initial hair growth
Initial hair growth
Elastase activity (10⁴ units/75 mm²)
Age (weeks)
0
1
2
3
4
4
6
8
10
12
14

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Declaration and Power of Attorney For Patent Application

特許出願宣言書及び委任状

Japanese Language Declaration

日本語宣言書

下記の氏名の発明者として、私は以下の通り宣言します。

As a below named inventor, I hereby declare that:

私の住所、私書箱、国籍は下記の私の氏名の後に記載された通りです。

My residence, post office address and citizenship are as stated next to my name.

下記の名称の発明に関して請求範囲に記載され、特許出願している発明内容について、私が最初かつ唯一の発明者（下記の氏名が一つの場合）もしくは最初かつ共同発明者（下記の名称が複数の場合）であると信じています。

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled.

"METHOD OF INHIBITING HAIR GROWTH"

上記発明の明細書は、

the specification of which

☒ 本書に添付されています。

☒ is attached hereto.

☐ ____月____日に提出され、米国出願番号または特許協定条約国際出願番号を_____とし、
（該当する場合）_____に訂正されました。

☐ was filed on _____
as United States Application Number or
PCT International Application Number
_____ and was amended on
_____ (if applicable).

私は、特許請求範囲を含む上記訂正後の明細書を検討し、内容を理解していることをここに表明します。

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

私は、連邦規則法典第37編第1条56項に定義されるとおり、特許資格の有無について重要な情報を開示する義務があることを認めます。

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

Japanese Language Declaration
(日本語宣言書)

私は、米国法典第35編119条 (a) - (d) 項又は365条 (b) 項に基づき下記の、米国以外の国の少なくとも一ヵ国を指定している特許協力条約365 (a) 項に基づく国際出願、又は外国での特許出願もしくは発明者証の出願についての外国優先権をここに主張するとともに、優先権を主張している、本出願の前に出願された特許または発明者証の外国出願を以下に、枠内をマークすることで、示しています。

I hereby claim foreign priority under Title 35, United States Code, Section 119 (a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)
外国での先行出願

(Number) (番号)	(Country) (国名)	(Day/Month/Year Filed) (出願年月日)	Priority Claimed 優先権主張 Yes はい	No いいえ
10-005959	Japan	14/January/1998	☒	☐
			☐	☐

私は、第35編米国法典119条 (e) 項に基づいて下記の米国特許出願規定に記載された権利をここに主張いたします。

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

(Application No.) (出願番号)	(Filing Date) (出願日)

私は、下記の米国法典第35編120条に基づいて下記の米国特許出願に記載された権利、又は米国を指定している特許協力条約365条 (c) に基づく権利をここに主張します。また、本出願の各請求範囲の内容が米国法典第35編112条第1項又は特許協力条約で規定された方法で先行する米国特許出願に開示されていない限り、その先行米国出願書提出日以降で本出願書の日本国内または特許協力条約国際提出日までの期間中に入手された、連邦規則法典第37編1条56項で定義された特許資格の有無に関する重要な情報について開示義務があることを認識しています。

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of application.

(Application No.) (出願番号)	(Filing Date) (出願日)	(Status: Patented, Pending, Abandoned) (現況：特許許可済、係属中、放棄済)
(Application No.) (出願番号)	(Filing Date) (出願日)	(Status: Patented, Pending, Abandoned) (現況：特許許可済、係属中、放棄済)

私は、私自信の知識に基づいて本宣言書中で私が行なう表明が真実であり、かつ私の入手した情報と私の信じるところに基づく表明が全て真実であると信じていること、さらに故意になされた虚偽の表明及びそれと同等の行為は米国法典第18編第1001条に基づき、罰金または拘禁、もしくはその両方により処罰されること、そしてそのような故意による虚偽の声明を行なえば、出願した、又は既に許可された特許の有効性が失われることを認識し、よってここに上記のごとく宣誓を致します。

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Japanese Language Declaration
(日本語宣言書)

委任状：私は下記の発明者として、本出願に関する一切の手続きを米特許商標局に対して遂行する弁理士または代理人として、下記の者を指名いたします。
(弁護士、または代理人の指名及び登録番号を明記のこと)

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